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U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: AAT/12387

US APPLICATION NO. (If known, see 37 CFR 1.5): 09/719944

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/GB99/01878	15 June 1999	16 June 1998

TITLE OF INVENTION: DIETARY SUPPLEMENT

APPLICANT(S) FOR DO/EO/US: GEORGIADES, Jerzy A.

OIPE DEC 15 2000 PATENT & TRADEMARK OFFICE

Applicant herewith submits to the United States Designated/Elected Office (DO/E O/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [ ] This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)).
4. [ ] The US has been elected by the expiration of 19 months from the priority date (PCT Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is attached hereto (required only if not communicated by the International Bureau).
   b. [X] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
7. [X] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [X] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 16 below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [X] Other items or information:

    Applicaton data sheet

430 Rec'd PCT/PTO 15 DEC 2000

U.S. APPLICATION NO. (if known, see 37 CFR 1 5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/719944	PCT/GB99/01878	AAT/12387

17. ☒ The following fees are submitted:

	CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1000.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$860.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$710.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$690.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 860.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☒ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	19 - 20 =	0	X **$18.00**	$ 0	
Independent claims	7 - 3 =	4	X **$80.00**	$ 320.00	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ **$270.00**	$	
TOTAL OF ABOVE CALCULATIONS =				$ 1,180.00	
☒ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.				$ 590.00	
SUBTOTAL =				$ 590.00	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☒ 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +				$	
TOTAL NATIONAL FEE =				$ 590.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				$	
TOTAL FEES ENCLOSED =				$ 590.00	
				Amount to be refunded:	$
				charged:	$

a. ☒ A check in the amount of $ 590.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. 18-0160 in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 18-0160. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pendin g status.

SEND ALL CORRESPONDENCE TO:

Customer No. 007609
Rankin, Hill, Porter & Clark LLP
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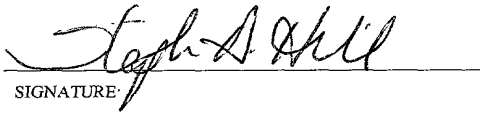

SIGNATURE

Stephen A. Hill
NAME

27,560
REGISTRATION NUMBER

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Georgiades, Jerzy A.
Title:	Dietary Supplement
International Application No.:	PCT/GB99/01678
International Filing Date:	15 June 1999
Attorney's Docket No.:	AAT/12387

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend the above identified application as follows:

IN THE CLAIMS

Amend claims 7, 8, 13 and 15 by substituting the following claims for the pending claims with the same number:

7. (amended) A baby food formula comprising a dietary supplement according to claim 1.

8. (amended) The use of dietary supplement according to claim 1 in a baby food formula.

13. (amended) A method of stimulating the immune system of a mammal, comprising administering a dietary supplement according to claim 1 in unit dosage form.

15. (amended) A method according to claim 13, wherein one unit dose of the dietary supplement is administered each day for a first period of not more than three weeks, then no dosage is administered for a subsequent period of up to three weeks.

Add new claims 16-19 as follows:

16. A baby food formula comprising a dietary supplement according to claim 5.

17. The use of dietary supplement according to claim 5 in a baby food formula.

18. A method of stimulating the immune system of a mammal, comprising administering a dietary supplement according to claim 5 in unit dosage form.

19. A method according to claim 14, wherein one unit dose of the dietary supplement is administered each day for a first period of not more than three weeks, then no dosage is administered for a subsequent period of up to three weeks.

REMARKS

By this amendment, claims 7, 8, 13 and 15 have been amended to eliminate multiple dependency, and new claims 16-19 have been added to present claim dependency eliminated in the amendment of claims 7, 8, 13 and 15.

New claim 16 corresponds to original claim 7 but is dependent on claim 5. New claim 17 corresponds to original claim 8 but is dependent on claim 5. New claim 18 corresponds to original claim 13 but is dependent on claim 5. New claim 19 corresponds to original claim 15 but is dependent on claim 14.

VERSION OF AMENDED CLAIMS WITH MARKINGS TO
SHOW CHANGES MADE

7. (amended) A baby food formula comprising a dietary supplement according to ~~any preceding~~ claim 1.

8. (amended) The use of dietary supplement according to ~~any preceding~~ claim 1 in a baby food formula.

13. (amended) A method of stimulating the immune system of a mammal, comprising administering a dietary supplement according to ~~any one of claims 1 to 6~~ claim 1 in unit dosage form.

15. (amended) A method according to claim 13 ~~or 14~~, wherein one unit dose of the dietary supplement is administered each day for a first period of not more than three weeks, then no dosage is administered for a subsequent period of up to three weeks.

Respectfully submitted,

Stephen A. Hill, Reg. No. 27,560
Attorney for Applicants

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December 15, 2000

DIETARY SUPPLEMENT

The present invention relates to a dietary supplement and, in particular, to a dietary supplement for promoting the functioning of the immune system. The invention also relates to baby formulas.

When a baby is born, its immune system is normally dormant and non-functioning but, as the baby grows, the immune system becomes active. There has recently been a hypothesis that mother's colostrum contains components which contribute to the awakening and development of the immune system. One particular such component is called colostrinin. It is found, inter alia, in ovine and human colostrum.

As a result of our studies, we have found that the administration of colostrinin to an infant may be of singular importance to the full development of the immune system, and that it is possible that an infant fed solely on bottle formula milk preparations may, as a result of not receiving colostrinin, have a poorly developed immune system. An imperfectly developed immune system can lead to the development of serious diseases such as atopic allergies including, for example, as asthma and skin allergies. There have even been reports that a reduced function of the immune system can lead to senility in old age and, possibly, to Alzheimer's disease.

It is impractical to solve this problem by trying to take steps to ensure that all infants are breast fed, because some mothers are physically unable to breastfeed, and others may not be able to breastfeed because they are undergoing treatment themselves and are taking drugs which should not be passed on to the baby through breast milk. Also, in some areas of the world, there is a social stigma attached to breastfeeding.

We have now devised a dietary supplement formula for promoting the correct functioning of the immune system. The supplement can be given to non-breast fed infants, for example by inclusion in their baby formulas or powdered milk feed. It can also be given to breast-fed infants, and to children and adults at any time of their life, especially if they show signs of immune deficiency. Thus, the invention provides a way of treating an individual with a view to promoting their immune system whether or not

they have been breast-fed, and whatever their state of health.

The dietary supplement of the present invention comprises colostrinin in combination with at least lactoferrin. We have found that this combination of substances exhibits synergism.

By "dietary supplement" we mean a preparation or formulation which is added to or otherwise included in a person's normal diet, and is present in addition to the normal diet. Thus, for example, a dietary supplement of the invention can be:

(a) in the form of a liquid or solid, eg. powder or as individual dosage units such as baby food formula, tablets or the like to be added to food or drinks, or taken with them;

(b) added to a foodstuff during its preparation, such as added to powdered milk feed for babies or otherwise included in children's and adults' foodstuffs.

By "dietary supplement" we do not intend to embrace foodstuffs per se that may naturally contain the components of the supplement according to the invention.

The synergism can be further enhanced by the addition of selenium to the composition.

The lactoferrin, selenium and colostrinin present in the preferred food supplement of the invention can each be of natural or synthetic origin, eg. produced by recombinant DNA technology. The supplements will normally also include a physiologically acceptable diluent or carrier such as is appropriate to the particular use intended.

In a preferred embodiment, the selenium is in the form of a physiologically acceptable selenoprotein, such as selenocysteine. The selenium can be provided in the form of glutathione peroxidase. The selenium can be provided in the form a complex in which it is bound to Lactobacillus acidophilus or yeast protein. Furthermore, the selenium protein complex is preferably human and may be from a recombinant or natural source. Selenium is known to be a weak inducer of the cytokines and in particular of gamma interferon. It is particularly preferred that the selenium be present in the dietary supplement in the form of selenium rich proteins rather than as a salt, since when administered as for example selenium picollinate, it is generally not fully utilised by the body.

The term "colostrinin", as used herein refers to a complex of polypeptides which, in its natural form, is obtained from any mammalian colostrum. Colostrum is the thick, yellowish fluid produced by a mammalian mother's breasts during the first few days after childbirth. It is the first lacteal secretion post parturition and it contains a high concentration of immunoglobulins (IgG, IgM and IgA) and nonspecific proteins. It is replaced by mature breast milk about four to five days after birth. Compared with mature breast milk, colostrum contains low sugar and iron. However, colostrum is richer in lipids, proteins, mineral salts, vitamins and immunoglobulins. It also contains various floating cells such as granular and stromal cells, neutrophils, monocyte/macrophages and lymphocytes and includes growth factors, hormones and cytokines.

Various factors have been isolated and characterised from mammalian colostrum. In 1974, Janusz et al (FEBS Lett., 49, 276-279) isolated a proline-rich polypeptide (PRP) from ovine colostrum. It has since been discovered that mammals other than sheep have analogues of PRP as a component of their colostrum. PRP has since been called colostrinin (and is sometimes called colostrinine).

M. Janusz & J. Lisowski in "Proline-Rich Polypeptide (PRP) - an Immunomodulatory Peptide from Ovine Colostrum" (Archivum Immunologiae et Therapiae Experimentalis, 1993, 41, 275-279) mentioned that PRP from ovine colostrum has immunotropic activity in mice.

A. Dubowska-Inglot et al in "Colostrinine: a proline-rich polypeptide from ovine colostrum is a modest cytokine inducer in human leukocytes" (Archivum Immunologiae et Therapiae Experimentalis, 1996, 44, 215-224) discussed the use of colostrinin in the treatment of Alzheimer's disease. The use of colostrinin in the treatment of Alzheimer's disease, and other conditions, was also discussed in WO-A-98/14473.

Colostrinin, in its natural form, is obtained from mammalian colostrum. As described in WO-A-98/14473, analysis by electrophoresis and chromatography has shown that colostrinin has the following properties:

(i) it has a molecular weight in the range 16,000 to 26,000 Daltons (this was shown by electrophoresis in the presence of SDS);

(ii) it is a dimer or trimer of sub-units each sub-unit having a

molecular weight in the range 5,000 to 10,000 Daltons (this was shown by acrylamide gel electrophoresis in the presence of SDS);

(iii) it contains proline, and the amount of proline is greater than the amount of any other single amino acid (this can be shown by conventional amino acid analysis).

It has also been shown that colostrinin and the sub-units making up the colostrinin are non-polar.

By means of these techniques it was shown that ovine colostrinin has a molecular weight of about 18,000 Daltons, is made up of three non-covalently linked sub-units each having a molecular weight of about 6,000 Daltons and includes about 22 wt% proline. The amino-acid composition of ovine colostrinin was shown to be made up of the following number of residues per sub-unit: lysine - 2, histidine - 1, arginine - 0, aspartic acid - 2, threonine - 4, serine - 3, glutamic acid - 6, proline - 11, glycine - 2, alanine - 0, valine - 5, methionine - 2, isoleucine - 2, leucine - 6, tyrosine - 1, phenylalanine - 3 and cysteine - 0.

The colostrinin used in the food supplement of the invention may be derived naturally from any mammalian source, such as humans, bovine, goats or sheep. Alternatively, the colostrinin may be made synthetically, for example, by recombinant DNA techniques. The colostrinin need not necessarily be in a pure form but may instead be, for example, partially purified as, for example, I_gG-colostrinin complex, or in a crude preparation form like whey, so long as the form is physiologically acceptable.

The source of the lactoferrin is also not critical but it should preferably be of bovine, ovine or human origin (or derived therefrom). Most preferably, human lactoferrin and/or human recombinant lactoferrin is used.

The preferred amounts of each ingredient per unit dose of the dietary supplement is as follows: colostrinin from about 12½ micrograms to about 200 micrograms; lactoferrin from about 10 micrograms to about 100 milligrams; and selenium, in the form of seleno-cysteine, from about 2.5 to about 100 micrograms. However, for young babies the preferred amount is below 2.5 micrograms, for example 0 to 1.0 micrograms.

The preferred dosage of the dietary supplement of the invention is one preferred

unit dose per day.

The dietary supplement of the invention may further include other biologically active substances such as the cytokines present in colostrum other than colostrinin, and hormones. For example, the supplement may include a natural cytokine preparation containing members of the interferon family (including interferon α and interferon γ), interleukin 1-α, interleukin 1-3, interleukin-6, 8, 10, 12, 16, tissue necrosis factor α, G-CSF (granulocyte colony stimulating factor), M-CSF (macrophage CSF), TGFα (transforming growth factor) and TGFβ.

The physiologically acceptable carrier of the dietary supplement of the present invention is chosen to be suitable for the intended use. Examples of suitable carriers include for example a solution of the hydrolysates of β casein in the form of 6.000 m.w. peptides, phosphate buffered saline (PBS), and whey.

The most preferred route for administering a dietary supplement of the invention is oral, especially in a form in which the supplement is maintained in contact with the oral and/or pharyngeal and/or intestinal tract mucosa. One preferred form is that of a baby food formula. Another preferred form is that of a lozenge, designed to be dissolved in the mouth. In the lozenge or other form, the dietary supplement may further include various flavouring or sweetening agents such as sucrose, mannose, lactose, maltose, trehalose, cold water soluble starch or other such ingredients known in the art.

As will be understood, the food supplement of the invention can be in a number of other forms such as powders, tablets, or liquid drinks and baby formulas. When in powder form, they can be added to a foodstuff such as, for example, a powdered milk formulation (or cheese or yoghourt or indeed any other foodstuff). The source of the milk is not important and may, for example, be cow, goat or sheep. The powdered milk formulation may be made up with a liquid to form a drink.

In another form, the dietary supplements of the invention can be included in a cheese. The source of milk forming the base of the composition to form the cheese is not important, but may include cow, goat or sheep.

The dietary supplement of the invention can also be added to the whey of goat, cow or sheep milk origin which whey may be obtained during cheese production. The

whey product containing the dietary supplement may be consumed as a drink.

In a further aspect of the present invention, there is provided the use of colostrinin in combination with lactoferrin in the manufacture of a medicament for bringing about an improvement in a individual's immune system.

The dietary supplement of the present invention can result, in adults, in an increase in energy and an apparent increase in clarity of thinking.

The dietary supplement of the invention should preferably not be used for more than 21 days continuously. This is because the phenomenon of tachyphylaxis may otherwise be induced. Tachyphylaxis is the gradual loss of an individual's capability to synthesise cytokines. In this situation an adverse reaction may be experienced. Induction of tachyphylaxis may be avoided by discontinuing the use of the dietary supplement of the invention after 21 days for a period of not less than 3 weeks. Following this brief pause, a new cycle of use can be initiated.

According to another aspect of the present invention there is provided a method of stimulating an individual's immune system, which method consists essentially of administering a dietary supplement of the present invention in unit dosage form, preferably each day for 21 consecutive days.

The invention described above relates to a dietary supplement containing colostrinin and lactoferrin, and to certain uses thereof. In another aspect the invention relates to a dietary supplement comprising colostrinin and selenium; this dietary supplement may be used in the same way as the dietary supplement described above, and may have the same additional components. In yet another aspect the invention relates to a dietary supplement comprising colostrinin and at least one of the cytokines listed above; this dietary supplement may be used in the same way as the dietary supplement described above, and may have the same additional components.

In order that the invention may be more fully understood, the following Examples are given by way of illustration only.

Example 1

Lozenge Formulation

The composition of a lozenge formulation of an example of the dietary

supplement of the invention per unit dose is as follows:

Ingredient	Amount
Sucrose, lactose or trehalose and/or	25 mg
Cold-water-soluble starch	42 mg
Phosphate Buffered Saline	(if required)
Natural colostrinin	100 μg
Selenium (metalloprotein) or other seleno-cysteine-containing proteins	5 μg
Purified recombinant human lactoferrin	10 mg

In all these examples, the colostrinin can be obtained by processes well known in the art. Such processes are described, for example, in the references discussed above. The other materials are also readily available.

Example 2

Method of manufacture of lozenge formulation

A starch gel-based lozenge containing colostrinin, lactoferrin and selenium is prepared by combining 150 g sucrose, 550 ml phosphate 0.15 mm buffered saline, and 250 g of cold-water-soluble starch such as that described in U.S. Patent 4,465,702, heating the mixture with stirring to a temperature of 75°C, cooling the mixture to 30°C and thereafter blending into the paste-like mass with 50 ml PBS containing 3 mg purified human colostrinin, 4.5 mg selenium (rich protein) and 300 mg purified recombinant human lactoferrin. The mixture is then formed into multiple portions of 5 to 10 grams each, which set upon standing under drying conditions to a starch candy gel-like consistency. The lozenges thereby produced can be administered to a patient singly or in combination. The patient is instructed to hold the lozenge in his mouth until it is completely dissolved to release the components for contact with the oral mucosa.

Example 3

Powdered Milk Formulation

A formulation for feeding to a baby post weaning from mother's milk, is:

Proprietary milk powder (e.g. Sma™, White™ by Sma Nutrition, Maidenhead, U.K. *)	4g **
Natural ovine colostrinin	150µg
Selenium (bound to lactobacillus acidophilus)	8.25µg (free selenium)
Human Recombinant Lactoferrin	1.0 mg

* Sma™ ingredients quoted as lactose, skimmed milk powder, vegetable oils, emulsifier (soya lecithin), potassium bicarbonate, vitamin C, taurine, ferrous sulphate, zinc sulphate, cytidine-5'-monophosphate, disodium uridine-5'-monophosphate, vitamin E, adenosine-5'-monophosphate, niacin, disodium inosine-5'-monophosphate, disodium guanosine-5'-monophosphate, pantothenic acid, vitamin A, copper sulphate, thiamin, vitamin B, riboflavin, beta-carotene, manganese sulphate, folic acid, vitamin K, potassium iodide, biotin, vitamin D, vitamin B. Although the manufacturer lists ferrous sulphate as an ingredient, we prefer not to include this material or any other iron containing compounds.

** Follow manufacturer's instructions for dosage guide e.g. weight 6.5 kg, approximate age of baby 4 months, 7 level scoops in 200 ml cooled (freshly boiled) water.

Example 4

Baby Food Formulas

The following formulations may be used for very young babies:

Formulas for new born 1 - 7 days old:

Natural Colostrinin (antibody - colostrinin complex)	50 µg per serving.
Lactoferrin	100 µg per serving.

(human recombinant or natural bovine)

Formulas for 8-14 days old babies:

Natural colostrinin	5.0 µg per serving.
Lactoferrin	100 µg per serving.
Selenium in form of seleno-cysteine	1.0 µg per serving.

Formulas for 15-30 days old babies.

Natural colostrinin	None
Lactoferrin	50 µg per serving.
Selenium	0.5 µg per serving.

Formulas for 31-45 days old babies.

Natural colostrinin complex	10 µg per serving.
Lactoferrin	50 µg per serving.
Selenium	0.5 µg per serving.

It will be appreciated that modifications may be made to the invention described above.

CLAIMS

1. A dietary supplement comprising colostrinin in combination with lactoferrin.

2. A dietary supplement according to claim 1, further comprising selenium.

3. A dietary supplement according to claim 1, wherein the selenium is in the form of a physiologically acceptable selenoprotein.

4. A dietary supplement according to claim 1, further comprising at least one cytokine selected from interferon α, interferon γ, interleukin 1-α, interleukin 1-3, interleukin 6, 8, 10, 12, 16, tissue necrosis factor α, G-CSF, M-CSF, TGFα and TGFβ.

5. A dietary supplement comprising colostrinin in combination with selenium.

6. A dietary supplement comprising colostrinin in combination with at least one cytokine selected from interferon α, interferon γ, interleukin 1-α, interleukin 1-3, interleukin 6, 8, 10, 12, 16, tissue necrosis factor α, G-CSF, M-CSF, TGFα and TGFβ.

7. A baby food formula comprising a dietary supplement according to any preceding claim.

8. The use of dietary supplement according to any preceding claim in a baby food formula.

9. A tablet, lozenge or other solid oral dosage form comprising 12.5 micrograms to 200 micrograms colostrinin, 10 micrograms to 100 milligrams lactoferrin, and 2.5 to 100 micrograms seleno-cysteine in combination with a physiologically acceptable carrier.

10. The use of colostrinin in combination with lactoferrin in the manufacture of a medicament for improving the immune system of mammals.

11. The use of colostrinin in combination with selenium in the manufacture of a medicament for improving the immune system of mammals.

12. The use of colostrinin in combination with at least one cytokine selected from interferon α, interferon γ, interleukin 1-α, interleukin 1-3, interleukin 6, 8, 10, 12, 16, tissue necrosis factor α, G-CSF, M-CSF, TGFα and TGFβ in the manufacture of a medicament for improving the immune system of mammals.

13. A method of stimulating the immune system of a mammal, comprising administering a dietary supplement according to any one of claims 1 to 6 in unit dosage form.

14. A method according to claim 13, wherein the unit dosage form comprises 12.5 micrograms to 200 micrograms colostrinin, 10 micrograms to 100 milligrams lactoferrin, and 2.5 to 100 micrograms seleno-cysteine in combination with a physiologically acceptable carrier.

15. A method according to claim 13 or 14, wherein one unit dose of the dietary supplement is administered each day for a first period of not more than three weeks, then no dosage is administered for a subsequent period of up to three weeks.

Please type a plus sign (+) inside this box → ☐

PTO/SB/01 (10-00)
Approved for use through 10/31/2002. OMB 0651-0032
U.S Patent and Trademark Office, U S DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)

☐ Declaration Submitted with Initial Filing **OR** ☒ Declaration Submitted after Initial Filing (surcharge (37 CFR 1.16 (e)) required)

Attorney Docket Number	AAT/12387
First Named Inventor	Georgiades, Jerzy A.
COMPLETE IF KNOWN	
Application Number	/
Filing Date	
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:

My residence, mailing address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

DIETARY SUPPLEMENT

(Title of the Invention)

the specification of which

☐ is attached hereto

OR

☒ was filed on (MM/DD/YYYY) 06/15/1999 as United States Application Number or PCT International Application Number PCT/GB99/01878 and was amended on (MM/DD/YYYY) _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached? YES	NO
9813031.3 /	United Kingdom	06/16/1998 /	☐	☐	☒
			☐	☐	☐
			☐	☐	☐
			☐	☐	☐

☐ Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

I hereby claim the benefit under 35 U.S.C. 119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)

☐ Additional provisional application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

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Kathryn A. Kelley

~~Attorney~~

30 April 2002

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NAME OF SOLE OR FIRST INVENTOR : ☐ A petition has been filed for this unsigned inventor

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☐ Additional inventors are being named on the ____supplemental Additional Inventor(s) sheet(s) PTO/SB/02A attached hereto.